

EXHIBIT 17

SPECIAL ARTICLE

Hospital Prices for Physician-Administered Drugs for Patients with Private Insurance

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ABSTRACT

BACKGROUND

Hospitals can leverage their position between the ultimate buyers and sellers of drugs to retain a substantial share of insurer pharmaceutical expenditures.

METHODS

In this study, we used 2020–2021 national Blue Cross Blue Shield claims data regarding patients in the United States who had drug-infusion visits for oncologic conditions, inflammatory conditions, or blood-cell deficiency disorders. Markups of the reimbursement prices were measured in terms of amounts paid by Blue Cross Blue Shield plans to hospitals and physician practices relative to the amounts paid by these providers to drug manufacturers. Acquisition-price reductions in hospital payments to drug manufacturers were measured in terms of discounts under the federal 340B Drug Pricing Program. We estimated the percentage of Blue Cross Blue Shield drug spending that was received by drug manufacturers and the percentage retained by provider organizations.

RESULTS

The study included 404,443 patients in the United States who had 4,727,189 drug-infusion visits. The median price markup (defined as the ratio of the reimbursement price to the acquisition price) for hospitals eligible for 340B discounts was 3.08 (interquartile range, 1.87 to 6.38). After adjustment for drug, patient, and geographic factors, price markups at hospitals eligible for 340B discounts were 6.59 times (95% confidence interval [CI], 6.02 to 7.16) as high as those in independent physician practices, and price markups at noneligible hospitals were 4.34 times (95% CI, 3.77 to 4.90) as high as those in physician practices. Hospitals eligible for 340B discounts retained 64.3% of insurer drug expenditures, whereas hospitals not eligible for 340B discounts retained 44.8% and independent physician practices retained 19.1%.

CONCLUSIONS

This study showed that hospitals imposed large price markups and retained a substantial share of total insurer spending on physician-administered drugs for patients with private insurance. The effects were especially large for hospitals eligible for discounts under the federal 340B Drug Pricing Program on acquisition costs paid to manufacturers. (Funded by Arnold Ventures and the National Institute for Health Care Management.)

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BALANCING THE COMPETING GOALS OF access and innovation is the central challenge facing public policy for the pharmaceutical sector. Drug prices in the United States are higher than in any other country. This situation leads to affordability challenges that reduce patient access. However, prices and the resulting revenues are used by manufacturers to finance a large share of research and development. There exists no fully satisfying resolution to the tension, although innovation can be supported with less reliance on prices as governmental programs extend their financial support from scientific research toward product development.¹ The balance of access and innovation can be furthered if the funds expended by payers accrue to pharmaceutical innovators with a minimum amount of diversion by intermediate entities. Diversion drives a wedge between the amounts paid for health care by employers, individual persons, and government programs, on the one hand, and the amounts received by drug manufacturers, on the other.

Pharmacy chains and pharmacy benefit managers divert a substantial fraction of spending on patient-administered drugs covered under Medicare Part D and employer pharmacy benefits. The scale of the diversion may be at least as much for physician-administered medications under Medicare Part B and employer medical benefits. The organizational intermediaries for physician-administered medications are composed of hospital outpatient departments and physician practices, which purchase the drugs from distributors and then obtain reimbursement from insurers in a process referred to as “buy and bill.” As hospitals have consolidated into large health systems, they have been able to increase the reimbursement prices they demand from insurers. Approximately one third of hospitals, including all specialized cancer hospitals, are also eligible for large discounts off drug acquisition prices under the federal 340B Drug Pricing Program.

Hospitals thus have two means to generate profits from physician-administered drugs. Hospitals can reduce what they pay to manufacturers for the drugs, especially if they are eligible for 340B discounts, and can increase what they are paid for the drugs by imposing markups on the reimbursement prices they charge to insurers.

Here, we report the results of a national study of hospital reimbursement-price markups to private Blue Cross Blue Shield (BCBS) insurers, 340B acquisition-price discounts to drug manufacturers, hospital revenues obtained owing to drug administration, and the allocation of insurer spending for physician-administered drugs between drug manufacturers and provider organizations. We also present data and findings on reimbursement prices, acquisition prices, and revenues for physician practices, which lack negotiating leverage with insurers and are not eligible for 340B acquisition-price discounts.

METHODS

DATA ON PATIENTS AND DRUGS

In this study, we used deidentified patient data from the 2020–2021 period from BCBS Axis, a data warehouse that includes claims involving approximately 50 million persons across the United States.² Claims were accessed for persons 18 to 64 years of age who were covered by employment-based insurance or individually purchased insurance. The BCBS Axis data do not include claims for patients who are covered by Medicaid or Medicare managed-care plans administered by the BCBS insurers. The data represent all firms in terms of size and include insured and self-insured employers, public agencies, and governmental entities. They also represent individual persons purchasing insurance directly through the Affordable Care Act exchanges.

The study focused on 36 infused drugs used primarily for oncologic conditions, 10 for inflammatory conditions, and 11 for blood-cell deficiency disorders.^{3,4} Drugs were selected from a list of physician-infused drugs that have been targeted for cost-reduction strategies by a large national insurer.⁵ Because that insurer did not target oncology drugs, we additionally selected oncology drugs on the basis of an analysis by the Employee Benefit Research Institute, an employer-sponsored organization, that identified drugs accounting for 80% of the total spending for infused drugs in commercially insured patients.³ The drugs are often used for multiple indications and, for this study, were classified according to their most prevalent use. The 57 products that were included in this study represent the most expensive physician-administered drugs, taking into

account both unit prices and volume of prescriptions. The drugs are listed in the Supplementary Appendix, which is available with the full text of this article at NEJM.org. The claims data that were used in this study cover drugs that are administered in hospital outpatient departments and physician practices and do not include drugs that are administered to hospital inpatients.

DATA ON REIMBURSEMENT PRICES

The prices in this study constitute the actual amounts paid by the insurer and collected by the hospital or physician practice, not the nominal list prices of the drugs. These infused drugs are not subject to the confidential rebates to payers that are prevalent for oral drugs and patient-injected drugs and that are managed by pharmacy benefit management firms. Infused drugs are sold by manufacturers and their wholesalers directly to hospitals, physician practices, and group purchasing organizations representing hospitals and physician practices. These provider organizations negotiate discounts with the manufacturers and thereby reduce the amount paid; the effect of these discounts is included in the claims data used in this study. This situation contrasts with how oral drugs and patient-injected drugs are distributed and reimbursed. For drugs that are administered by patients, the manufacturers and their wholesalers sell to retail and mail-order pharmacies. Pharmacy benefit managers then negotiate confidential rebates with the manufacturers, as a condition for inclusion in the formulary. The value of the negotiated rebates is shared among the insurers, employers, and pharmacy benefit managers, although typically not with the patients, who are responsible for cost-sharing. The scale of these so-called off-invoice rebates is not measured in claims data. This limitation on claims data does not affect the present study, given that we focused on physician-administered drugs rather than on patient-administered drugs.

Two types of prices are charged for the physician-administered drugs that are distributed directly to hospitals and physician practices. These providers purchase the drugs from manufacturers and wholesalers at what is referred to as the “acquisition price.” The providers then charge a different, and typically higher, “reimbursement price” to the patient’s insurer. The difference between the reimbursement price and the acquisition

price is retained by the provider organization as its revenue on the drug sale.

The measure of reimbursement price that we used in this study was calculated by dividing the total paid amount on each insurance claim by the number of drug units administered to the patient during the infusion visit. The reimbursement price reflects the amount paid for the infused drug and not the amount charged for the clinical work of administering the drug to the patient, which is paid separately.

DATA ON ACQUISITION PRICES

The acquisition price that is paid by each hospital to the manufacturer is not reflected on the insurance claim and was estimated for this study on the basis of the average sales price as calculated by the Centers for Medicare and Medicaid Services (CMS) to reimburse drugs under Medicare Part B. CMS requires drug manufacturers to report net revenues for each drug, which are calculated after accounting for all discounts and rebates to insurers, wholesalers, distributors, specialty pharmacies, mail-order pharmacies, retail pharmacies, and other supply-chain intermediaries. The average sales price is an accurate measure of the average acquisition price that is paid by providers to drug manufacturers but, being an average, overestimates the acquisition prices paid by some and underestimates the prices paid by others. CMS pays all hospitals and physician practices the same rate for the same drug, which is the average sales price plus a 6% additional margin to cover the costs of inventory and handling.⁶

Nationwide, approximately one third of hospitals and their outpatient departments are eligible for discounts on the acquisition prices they pay to drug manufacturers through the federal 340B Drug Pricing Program. The 340B Program was designed to ensure that hospitals and outpatient clinics serving low-income patients could afford expensive drugs, but it has evolved so that eligible organizations can obtain the acquisition-price discounts even on drugs infused in patients who are covered by private insurers or Medicare. CMS has estimated that the acquisition prices paid to drug manufacturers by hospitals eligible for 340B discounts equal 65% of the average sales price.^{7,8} For this study, hospitals eligible for 340B discounts were identified by means of data from the Health Resources and Services Administration,

Table 1. Patient Visits for Drug Infusion, According to Care Setting and Therapeutic Category.*

Variable	Hospitals Eligible for 340B Discounts	Hospitals Not Eligible for 340B Discounts	Independent Physician Practices
No. of care sites	1446	2341	28,719
No. of infusion visits	1,157,693	685,062	2,884,434
Distribution of drug infusions (%)			
For oncologic conditions	81.5	82.9	62.5
For inflammatory conditions	9.5	5.0	29.3
For blood-cell deficiency disorders	9.0	12.1	8.2
Mean age of the patient (yr)	51.6	57.2	51.0
Female sex (%)	56.2	59.6	59.4

* Data are compared among hospitals that are eligible for acquisition-price discounts under the federal 340B Drug Pricing Program, hospitals that are not eligible for the program, and independent physician practices (which are also not eligible).

which oversees the program. To be consistent with CMS guidance, we used a value of 0.65 times the average sales price as the estimated drug acquisition price for hospitals eligible for 340B discounts. For hospitals not eligible for 340B discounts and for physician practices, we used the average sales price as the measure of the drug acquisition price.⁹

STATISTICAL ANALYSIS

We calculated the ratio of the reimbursement price to the acquisition price for each drug, which was assessed as the median markup (and interquartile range) across hospitals eligible for 340B discounts, noneligible hospitals, and physician practices. Price markups were calculated at the claim level and aggregated to the level of the hospital and physician practice. The median markup was calculated individually for each of the drugs in the three major therapeutic classes (oncologic conditions, inflammatory conditions, and blood-cell deficiency disorders).

Multivariable regression models were used to analyze differences across hospitals eligible for 340B discounts, noneligible hospitals, and physician practices in the reimbursement prices charged and the revenues retained by providers. Covariates included patient age and sex, indicators for each of the 57 drugs, indicators for geographic location as measured by the 306 hospital referral regions in the United States, and the year and month of the drug-infusion visit. The multivariable analysis was conducted with the use of generalized least-squares model

regressions with a log-transformed link function and a gamma-distributed error term, with standard errors clustered at the drug level. Absolute differences and markups in price were calculated from marginal price effects.

The revenues that were retained by hospitals and physician practices were calculated both in terms of U.S. dollars and as a percentage of total insurer spending on these infused drugs in each of the three care settings (hospitals eligible for 340B discounts, noneligible hospitals, and physician practices). We calculated the total insurer spending in each hospital and physician practice by summing the amount paid from all the claims for all 57 drugs. Total spending at the level of the hospital and the physician practice was calculated as the sum of the number of units administered, multiplied by the acquisition price per unit, for all 57 drugs. Insurer reimbursement spending and provider acquisition spending for each hospital and physician practice were then summed for each of the three categories of providers studied, including hospitals eligible for 340B discounts, noneligible hospitals, and physician practices.

RESULTS

DESCRIPTIVE STATISTICS

Table 1 presents the number of care sites, the number of patient visits for infusion, and the percentage of patient visits for each of the three major therapeutic conditions. The 404,443 patients who were included in the study had

Table 2. Median Ratio of Drug Reimbursement Price to Drug Acquisition Price for Hospitals and Physician Practices.

Drug Type	Hospitals Eligible for 340B Discounts	Hospitals Not Eligible for 340B Discounts	Independent Physician Practices
	<i>median ratio (interquartile range)</i>		
All drugs	3.08 (1.87–6.38)	2.44 (1.40–4.95)	1.12 (1.02–1.63)
Drugs for oncologic conditions	3.19 (1.94–7.07)	2.48 (1.42–5.23)	1.13 (1.02–1.81)
Drugs for inflammatory conditions	2.26 (1.63–3.98)	1.54 (1.08–2.99)	1.07 (1.00–1.23)
Drugs for blood-cell deficiency disorders	2.95 (1.88–4.73)	2.57 (1.58–4.44)	1.20 (1.04–1.76)

4,727,189 infusion visits during the 2020–2021 period. These infusions were administered at 32,506 sites of care, of which 4.4% were hospitals eligible for 340B discounts, 7.2% were non-eligible hospitals, and 88.3% were community-based physician practices. Hospitals eligible for 340B discounts accounted for 24.5% of all the infusions, whereas noneligible hospitals accounted for 14.5% and physician practices for 61.0%. Drugs for oncologic conditions were most common in the study sample, accounting for 81.5% of the infusions in hospitals eligible for 340B discounts, for 82.9% of those in noneligible hospitals, and for 62.5% of those in physician practices.

PRICES AND PRICE MARKUPS

Table 2 presents the distribution of drug-price markups, assessed as the ratio of the reimbursement price to the acquisition price, for drugs in each of the three therapeutic classes and in each of the three care settings. For drugs to treat oncologic conditions, the median markup ratio across hospitals eligible for 340B discounts was 3.19 (interquartile range, 1.94 to 7.07); for drugs to treat inflammatory conditions, the median markup ratio was 2.26 (interquartile range, 1.63 to 3.98), and for drugs to treat blood-cell deficiency disorders, it was 2.95 (interquartile range, 1.88 to 4.73). For hospitals not eligible for 340B discounts, the median markup for drugs to treat oncologic conditions was 2.48 (interquartile range, 1.42 to 5.23), for drugs to treat inflammatory conditions 1.54 (interquartile range, 1.08 to 2.99), and for drugs to treat blood-cell deficiency disorders 2.57 (interquartile range, 1.58 to 4.44). For physician practices, the median markups were 1.13 (interquartile range, 1.02 to 1.81) for drugs to treat oncologic conditions, 1.07 (interquartile range, 1.00 to 1.23) for drugs to treat inflamma-

tory conditions, and 1.20 (interquartile range, 1.04 to 1.76) for drugs to treat blood-cell deficiency disorders.

The median price markups for each of the individual 57 drugs are shown in Figure 1, which shows the ratio of the reimbursement price to the acquisition price in each of the three care settings. Reimbursement-price markups above acquisition prices varied widely across drugs and care settings but were consistently higher in hospital outpatient clinics than in physician offices. There was little variability in the price markups for physician practices, as shown by the almost horizontal alignment of those prices in Figure 1, given that physicians lack the bargaining leverage used by some hospital systems to increase prices charged to insurers. Table S1 in the Supplementary Appendix presents reimbursement-price markups for each of the individual drugs across each of the three care settings.

MULTIVARIABLE REGRESSION ANALYSIS

The data in Table 3 compare the relative prices charged, the absolute prices charged, and the price markups by hospitals relative to community-based physician practices. These data differentiate between hospitals that are eligible and those that are not eligible for the 340B Program and were adjusted for patient demographic characteristics, drug, month and year of drug infusion, and geographic market. Hospitals eligible for 340B discounts charged reimbursement prices to insurers that averaged 289.2% (95% confidence interval [CI], 221.2 to 371.5) above those charged by physician practices, whereas hospitals not eligible for the 340B Program charged insurers prices that were 276.0% (95% CI, 205.3 to 363.5) above those charged by physician practices. The similarity in the reimbursement-price markups across the two sets of hospitals, despite the fact that hospitals

Table 3. Multivariable Regression–Adjusted Differences in Drug Acquisition Prices, Price Markups, and Retained Drug Expenditures in Hospitals as Compared with Independent Physician Practices.*

Variable	Hospitals Eligible for 340B Discounts	Hospitals Not Eligible for 340B Discounts
Percentage difference in reimbursement price charged to insurers by hospitals vs. reimbursement price charged by physician practices (95% CI) — %	289.2 (221.2–371.5)	276.0 (205.3–363.5)
Dollar difference in reimbursement price charged by hospitals vs. reimbursement price charged by physician practices (95% CI) — U.S. \$	650.24 (448.97–851.50)	633.90 (437.07–830.67)
Ratio of hospital markup of drug reimbursement price over acquisition price to reimbursement price markups by physician practices (95% CI)	6.59 (6.02–7.16)	4.34 (3.77–4.90)

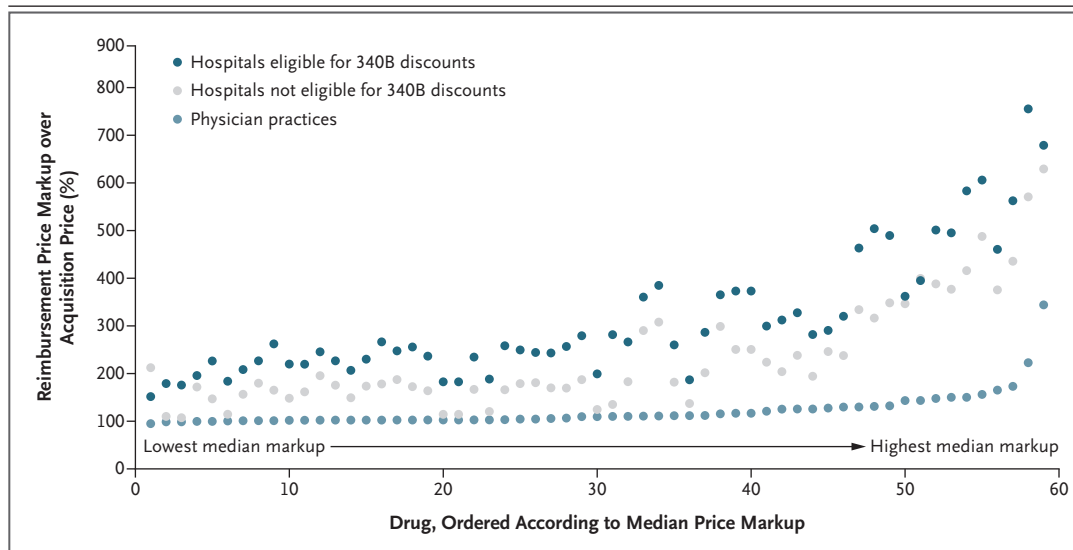
* Regressions were adjusted for patient demographic characteristics and included indicators for the 57 drugs, the month and year of each infusion visit, and hospital referral regions. Regression coefficients were calculated by means of general linear model regressions with a log-transformed link function and a gamma-distributed error term. Prices were measured in terms of the amount paid for the drug used in the infusion visit, divided by the number of drug units infused. CI denotes confidence interval.

eligible for 340B discounts have drug acquisition prices that are 35% lower than the acquisition prices at noneligible hospitals, indicates that the eligible hospitals are not passing on to insurers the value of the acquisition-price discounts.

Table 3 also shows differences between hospitals and physician practices in the absolute reimbursement price per drug unit. Hospitals eligible

for 340B discounts earned \$650.24 (95% CI, 448.97 to 851.50) more per drug unit than did independent physician practices. Hospitals not eligible for 340B discounts earned \$633.90 (95% CI, 437.07 to 830.67) per drug unit above that earned by physician practices.

There were major differences between the two categories of hospitals with regard to their

**Figure 1.** Drug Price Markups above Acquisition Prices in Hospitals Eligible for 340B Discounts, Hospitals Not Eligible for 340B Discounts, and Independent Physician Practices.

The 57 drugs that were used in hospital outpatient departments and physician practices and were included in the study are arrayed along the horizontal axis according to the median price markup in hospitals eligible for acquisition-price discounts under the federal 340B Drug Pricing Program. The data underlying this figure are presented in the Supplementary Appendix.

Table 4. Percentage of Insurer Spending on Infused Drugs That Is Retained by Hospitals and Physician Practices.

Drug Type	Hospitals Eligible for 340B Discounts	Hospitals Not Eligible for 340B Discounts	Independent Physician Practices
	<i>percent</i>		
All drugs	64.3	44.8	19.1
Drugs for oncologic conditions	64.6	50.0	17.3
Drugs for inflammatory conditions	68.0	55.2	19.0
Drugs for blood-cell deficiency disorders	55.8	9.1	29.8

ability to impose reimbursement-price markups over the acquisition prices they pay to drug manufacturers (Table 3). Hospitals eligible for 340B discounts obtained reimbursement-price markups that were 6.59 times (95% CI, 6.02 to 7.16) as high as those obtained by physician practices. Hospitals not eligible for the 340B Program obtained markups that were 4.34 times (95% CI, 3.77 to 4.90) as high as those obtained by physician practices, after adjustment for other relevant factors. This difference in the markups above acquisition prices was due to the much lower acquisition prices paid by hospitals eligible for 340B discounts.

RETENTION OF INSURER DRUG SPENDING BY PROVIDERS

Table 4 shows the percentages of insurer drug spending that were retained by hospitals and physician practices rather than flowing to the drug manufacturers. The BCBS reimbursement-price markups are independent of the 340B acquisition-price discounts, but both influence the revenue retained from drug infusion at hospitals and physician practices. The highest revenues were obtained by hospitals that obtained both BCBS reimbursement-price markups and 340B acquisition-price discounts, followed by hospitals that obtained BCBS reimbursement-price markups but were not eligible for 340B acquisition-price discounts. The lowest revenues were accrued by physician practices that obtain neither BCBS reimbursement-price markups nor acquisition-price discounts in the 340B Program. Hospitals eligible for 340B discounts retained 64.6% of insurer spending for drugs to treat oncologic conditions, 68.0% of that for drugs to treat inflammatory conditions, and 55.8% of that for drugs to treat blood-cell deficiency disorders; noneligible hospitals retained 50.0%, 55.2%, and

9.1%, respectively, and physician practices retained 17.3%, 19.0%, and 29.8%, respectively.

DISCUSSION

This analysis of data regarding patients with private BCBS insurance quantifies the reimbursement-price markups, the acquisition-price discounts, and the resulting revenues retained from physician-administered infused drugs for hospitals as compared with physician practices. This study extends previous analyses of drug prices and spending across care settings that did not disentangle the effects of unit prices, drug selection, and dose regimens.^{3,4,10-12} After adjustment for differences across drugs, patient demographic characteristics, and geographic regions, we found that hospitals eligible for federal 340B discounts charged reimbursement prices to insurers that were 289% above those charged by physician practices, whereas hospitals not eligible for 340B discounts charged reimbursement prices 276% above those charged by physician practices. The markup of reimbursement prices charged to insurers over the acquisition prices paid to drug manufacturers highlights the importance of payer mix to hospitals and physician practices, given that Medicare pays a markup above the acquisition price of only 6%.

The diversion of pharmaceutical spending is not limited to physician-administered medications distributed by hospitals but includes patient-administered oral and injectable drugs that are distributed through retail pharmacies. The percentage of insurer spending on these drugs that accrues to pharmaceutical companies has been decreasing over time. For every \$100 spent on retail drugs in 2015, for example, only 58% accrued to the manufacturer and the remainder to intermediaries.¹³ Only half the amount spent on

insulin by insurers in 2018 was collected by manufacturers, down from 70% in 2014.¹⁴

The results reported here should be interpreted with consideration of the limitations of the study. The study was limited to patients enrolled in BCBS plans in the United States and may not be representative of the entire population nationwide. We do not have information on the income level of the patients included in this study. The BCBS plans account for the largest share of enrollment in commercial insurance, covering public and private employers, insured and self-insured firms, and persons purchasing coverage through health insurance exchanges established by the Affordable Care Act. As such, these data represent the range of income levels for persons covered by private insurance. The data do not represent the experience of the poorest patients, who tend to be covered by Medicaid plans. We do not have information on the cost-sharing requirements facing individual patients included in the study, but the BCBS plans cover the full range of plan designs, including plans with comprehensive coverage and those with high deductibles. The study also did not include data on patients who are covered by Medicare. We used the Medicare average sales price to estimate the acquisition price paid by

hospitals and physician practices for infused drugs, with adjustment according to eligibility for 340B discounts. The average-sales-price formula of Medicare represents the average acquisition price for the hospitals and physician practices that purchase the drug but does not represent the acquisition price negotiated by each individual facility, which varies around this average.¹⁵

Hospitals impose reimbursement-price markups to private insurers for the infused drugs that are administered in their outpatient departments. Facilities that are covered by the federal 340B Drug Pricing Program also receive acquisition-price discounts on the amounts they pay to drug manufacturers. The difference between the reimbursement price charged to insurers and the acquisition price paid to manufacturers can be substantial. In this study, we found that hospitals that imposed both price markups to insurers and 340B discounts to manufacturers retained almost two thirds of insurer drug expenditures, passing on only one third to the drug companies.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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